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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,958	01/31/2005	Clarence W Andrews III	PU4870USW	6658
23347	7590	08/27/2007		
GLAXOSMITHKLINE CORPORATE INTELLECTUAL PROPERTY, MAI B475 FIVE MOORE DR., PO BOX 13398 RESEARCH TRIANGLE PARK, NC 27709-3398			EXAMINER LOEWE, SUN JAE Y	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 08/27/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/522,958	Applicant(s) ANDREWS ET AL.	
	Examiner Sun Jae Y. Loewe	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21, 23, 25-30, 43, 44 and 46 is/are pending in the application.
- 4a) Of the above claim(s) 25-30, 44 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 21, 23 and 43 is/are rejected.
- 7) ☒ Claim(s) 20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date
:8/24/07,6/13/06,4/26/06,2/9/06,1/31/05.

DETAILED ACTION

Election/Restrictions

1. Based on the proposal submitted by the Applicant, the restriction requirement dated August 6, 2007 is modified to the following:

Group I: claims 1-23, 43, 44, and 46 drawn to compounds of formula (I) wherein Q² is defined as a group of formula: $-(R^2)_{a1}-(Y^2)_{b1}-(R^2)_{c1}-R^4$, i.e., two adjacent Q² groups together with the carbon atoms to which they are bound, do not form a further ring fused to the benzimidazole.

Group II: claims 1-23, 43, 44, and 46 drawn to compounds of formula (I) wherein two adjacent Q² groups together with the carbon atoms to which they are bound, do form a further ring fused to the benzimidazole.

Group III: claims 25-29 drawn to a method of using compounds of Group I.

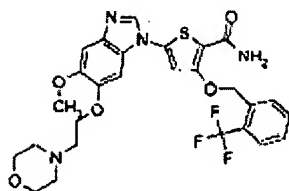
Group IV: claims 25-29 drawn to a method of using compounds of Group II.

Group V: claim 30 drawn to a process for preparing compounds of Group I.

Group VI: claim 30 drawn to a process for preparing compounds of Group II.

The requirement for an election of species within each of Groups I-VI is maintained. The revised restriction requirement (above) is made FINAL

2. Applicant's election without traverse Group I (above) and compound of example 137



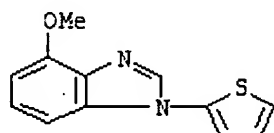
in the reply filed on August 15, 2007 is acknowledged.

3. Claims 25-30 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on August 15, 2008.

3. MPEP § 803.02 provides guidelines for election of species in Markush-type claims.

These guidelines were followed for the search and examination detailed herein.

The elected species appeared to be allowable over the art of record, therefore the search and examination was extended to the non-elected species of:



This compound was found to be anticipated by the prior art (below, Section 9), thus Markush-type claims were rejected and the subject matter drawn to nonelected species held withdrawn from further consideration (ie. claims 44 and 46, in addition withdrawn claims listed in Section 3).

Claims 1-21, 23 and 43 were further examined, pursuant to MPEP § 803.02, to the extent necessary to determine patentability. The search was limited to the elected species and the non-elected species identified above.

It has been determined that the entire scope claimed is not patentable.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted (January 31, 2005; February 9, 2006; April 4, 2006; June 13, 2006; August 15, 2007) were in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the information disclosure statements were considered. Signed copies of form 1449 are submitted herewith.

Claim Objections

5. Claims 1-21, 23 and 43 objected to for containing non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Written Description)

6. Claims 1-19, 21, 23 and 43 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

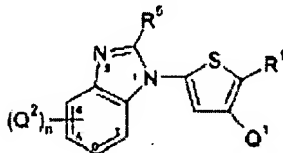
“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...”) *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, “Written Description” Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. Scope of Claims (based on Group I of Section 1)

Compounds of Formula I.



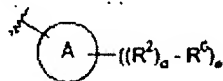
The following variables are claimed broader than what is supported by the disclosure (see below section II): Q^1 and Q^2 .

II. Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice do not support the following definitions for Q^1 and Q^2 .

group of formula (ii)



wherein ring A is not pyrrolidine, imidazoline, thiophene, furan, cyclohexyl, piperazine, piperidine, tetrahydropyran, morpholine, benzodioxolane and/or

wherein R^6 is a substituent that contains a ring other than phenyl

Reduction to Structural or Chemical Formulas:

The only disclosure, in addition to the species reduced to practice, is in form of lists of possible groups (eg. thietane, thiomorpholine, thiazolidine, oxazolidine, for heterocycle).

This type of disclosure is not viewed to be a representation of any of the species it entails.

A "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Therefore, there is no

disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

A structure activity study is disclosed by M. Cheung

M. CHEUNG; "Discovery of Novel Polo-like Kinase 1 (PLK-1) Inhibitors"; Natural Products Gordon Research Conference.; 22-27 July 2007;). This study addresses the effect on activity upon variation of substituents including Q¹ and Q². The disclosure, however, does not address the SAR commensurate in scope with the structural broadness of the variables instantly claimed. For example, Q1 was varied only within the boundaries of alkyl, haloalkyl, and halo. Nonetheless, the disclosure does affirm that the activity is influenced by changing the nature of Q1 and Q2. The instant specification does not provide further guidance and/or a structure activity correlation. Therefore, it is not understood what specific structural elements (pertaining to variables Q¹ and Q²) are essential for the activity of the instantly claimed compounds (see further discussion below section 7).

III. Analysis of Fulfillment of Written Description Requirement:

In the absence of a correlation between structure and function (with scope commensurate with that instantly claimed), it is not possible to determine which structural modifications will lead to compounds that are inhibitors of polo-like kinase.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-19, 21, 23 and 43; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

7. Claims 1-19, 21, 23 and 43 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for the use of the compounds that have adequate written description. The specification is not enabling for the use of compounds not supported by the disclosure. In conclusion, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims

Compounds not supported by the disclosure (see above section 6.I and 6.II.).

The nature of the invention

The compounds are disclosed to be polo-like kinase (PLK) inhibitors.

The state of the prior art/level of ordinary skill/level of predictability

The level of ordinary skill is high, but the level of predictability in the art is low. As discussed in section 6, it is not known what structural limitations (ie. for variables Q¹ and

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Q²) are required for preservation of activity within the genus claimed. Furthermore, it is noted that the activity of the instantly claimed compounds appears to vary substantially with changes to the nature of Q¹ and Q² (Cheung et al.,

M. CHEUNG; "Discovery of Novel Polo-like Kinase 1 (PLK-1) Inhibitors"; Natural Products Gordon Research Conference.; 22-27 July 2007;

). Thus, one of ordinary skill would not be able to predict what structural modifications within the unrepresented genus (ie. unrepresented by the disclosure), if any, would lead to compounds that are inhibitors of PLK.

The amount of direction provided by the inventor/existence of working examples

No direction or working examples.

The quantity of experimentation needed to make or use the invention

It is not known which of the unrepresented compounds meet the structural requirements for activity. Thus, one of ordinary skill would not be enabled by the disclosure to make/use the claimed PLK inhibitors. The amount of experimentation needed to practice the invention is deemed to be undue.

Claim Rejections - 35 USC § 112 2nd Paragraph

8. Claim 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites "Y² is -O-, -N(R⁷)CO₂- and -N(R⁷)C(O)N(R⁷)-. ". It appears that the word "and" should be replaced by "or". Alternatively, variable Y² should be written in proper Markush format.

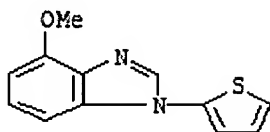
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 15-19 and 21 rejected under 35 U.S.C. 102(b) as being anticipated by Palmer et al.



The reference teaches

(page 6569, compound 94): $R^1=R^5=H$;

$Q^1=-(R^2)_a-(Y^1)_b-(R^3)_c-R^3$ wherein $a=b=c=0$ and $R^3=H$; $Q^2=-(R^2)_{aa}-(Y^2)_{bb}-(R^3)_{cc}-R^4$ wherein $aa=cc=0$, $bb=1$, $Y^2=-O-$ and $R^4=Me$.

Conclusion

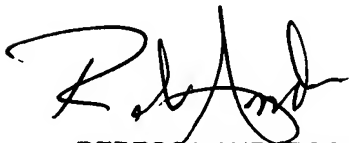
10. No claims allowed.
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe, Ph.D.
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A handwritten signature in black ink, appearing to read 'Rebecca Anderson', with a stylized, cursive script.

REBECCA ANDERSON
PRIMARY EXAMINER